REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated January 28, 2003 are respectfully requested. A separate petition for a 3-month extension of time accompanies this amendment. Claims 1-8, 11, 25, 26, 29, 31-34, 37, 39 and 40 are currently under examination.

I. Amendments

Claim 3 has been amended to overcome a rejection under 35 U.S.C. § 112, second paragraph, as discussed below. Claims 12, 30 and 38 have been cancelled, without prejudice.

No new matter has been added by this amendment.

II. Objections

Claims 12, 30 and 38 were objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. These claims have been cancelled, thereby obviating the objection.

III. Rejections under 35 U.S.C. § 112, second paragraph

Claims 11-13 and 17 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 11 and 17 were rejected for lacking antecedent basis for the terms "the lipid bilayer expanse" and "the form," respectively.

Claim 1 has been rejected for being open-ended and not excluding additional unrecited elements or steps.

An Examiner must clearly define the problem and why it is a problem in connection with the issue of claim definiteness in order to provide an applicant or any reviewing authority with the information necessary to evaluate the Examiner's position fairly. Applicants submit that the rejection fails to establish a prima facie case of indefiniteness. The MPEP provides the following: "The examiner's focus during examination of claims for compliance with the requirement for definiteness ... is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available." *MPEP* §2173.02. The Examiner must clearly and fully state the grounds of the rejection. Absent specific rejections and explanations of indefiniteness, Applicants fail to see where the claim lacks clarity or definiteness. If the Examiner is asserting that the claim is too broad, Applicants traverse the rejection in view of the CCPA's decision that "[a]n applicant is entitled to claims as broad as the prior art and his disclosure will allow." *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323, 326 (C.C.P.A. 1981). The breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597, 600 (C.C.P.A. 1971). Thus, the Examiner may not reject claim 1 as indefinite merely because is too broad.

Accordingly, Applicants submit that the presently pending claims satisfy the requirements of 35 U.S.C. §112, second paragraph.

IV. Rejections under 35 U.S.C. § 112, first paragraph

Claim 1 stands rejected under 35 U.S.C., first paragraph on the ground that the specification lacks adequate written description to support the claims. It is the Examiner's position that the disclosure in the specification does not reasonably convey to one of ordinary skill in the art that the inventors had possession of the claimed invention at the time the application was filed.

More specifically, the Examiner has rejected the claims as broadly directed to encompass DNA encoding a protein effective to inhibit cell apoptosis in cells characterized by a high level of cytokine production, and that the claim is directed to encompass any and all DNAs encoding any and all proteins that inhibit any and all apoptotic mechanisms.

The Examiner has cited no case law in support of his postion, and the only case law on this issue is applicable to claims directed to new biological molecules that can be represented as sequences, or to novel compositions containing such new biological molecules. There is no case law that Applicants are aware of that is applicable to claims in which known and readily obtainable sequences are employed. Nor are the applicants aware of any case law pertinent to the written-description requirement that would require an applicant to identify all known and easily obtained sequences used in characterizing a claimed composition.

In view of the fact that the presently pending claims employ recombinant elements that are known and/or easily obtained by standard methods, as discussed in the specification on at least page 23, lines 26-30 and page 26, lines 8-11, the Examiner's rejection of claim 1 for failure to meet the written description requirement of §112, first paragraph, finds no basis in the law.

Accordingly, Applicants request that the rejection of the claim based on the written description requirement of 35 U.S.C. §112, first paragraph, be withdrawn.

V. Rejection under 35 U.S.C. §102(b)

Claim 3 was rejected under 35 U.S.C. §102(b) as being anticipated by Dixit (U.S. Patent No. 6,159,712).

These rejections are respectfully traversed in view of the foregoing claim amendments and following remarks.

A. Legal Standard for Anticipation.

For a prior art reference to be anticipating under 35 U.S.C. §102, it must teach "each and every" element of the claimed invention. *In re Bond,* 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). "Anticipation requires identity of invention: the claimed invention, as described in appropriately construed claims, must be the same as that of the reference, in order to anticipate." *Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc.,* 33 USPQ2d 1496 (Fed. Cir. 1995).

Applicants submit that none of the cited references meets the legal standard of anticipation for the reasons set forth below.

B. Key Claim Limitations of the Presently Claimed Invention

The present invention, as embodied in claim 3 includes a human cell line prepared by the process including obtaining a parental human cell line capable of producing one or more cytokines; modifying the cells by introducing an expression vector comprising the coding sequence for CrmA operably linked to a first promoter, and additional control elements necessary for expression in human cells, into the cells of said cell line; and screening and selecting for CrmA-expressing cells. A key limitation of the claim is that the human cell line is for use in producing one or more cytokines.

C. Rejection over Dixit

Dixit discloses methods and compositions for decreasing apoptosis using CrmA. The cell lines described in Dixit, however, are not used for producing cytokines. The modifications proposed to the cell lines described by Dixit are for maintaining *in vivo* viability to the maximum extent possible such that the cells are useful for inhibiting infections, e.g. HIV. As taught throughout Dixit, cytokines such as TNF cause cell death, which is an undesirable event for maintaining *in vivo* viability. Dixit discloses that cells transfected with CrmA inhibit apoptosis, but nowhere does Dixit disclose that CrmA completely prevents apoptosis such that more cytokine production would be desirable, or even acceptable, in any way.

Thus, Dixit does not disclose a critical feature, and therefore cannot anticipate the presently claimed invention. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §102(b).

VI. Rejection under 35 U.S.C. §103(a)

Claims 1-8, 11, 12, 25, 26, 29-34 and 37-40 were rejected under 35 U.S.C. §103(a) as being unpatentable over Dixit (U.S. Patent No. 6,159,712) in view of Lau *et al.* (U.S. Patent No. 6,159,712).

A. The Invention

The present invention, as embodied in claims 1 and 3, includes a a human cell composition or cell line for use in producing one or more cytokines. The cell composition of claim 1 includes a human cell line characterized by expression of the coding sequence for an anti-apoptotic protein and a level of cytokine production that is at least two times (2X) the level of cytokine production exhibited by a corresponding parental cell line that does not express the coding sequence for the anti-apoptotic protein.

The cell line of claim 3, as described above, is prepared by a process that includes obtaining a parental human cell line capable of producing one or more cytokines; modifying the cells by introducing an expression vector comprising the coding sequence for CrmA operably linked to a first promoter, and additional control elements necessary for expression in human cells, into the cells of said cell line; and screening and selecting for CrmA-expressing cells.

B. The Cited Art

Dixit is described above.

Lau discloses methods for enhancing the production of interferons in animal cell culture. Inducers, such as PKR, are used to increase levels of the interferons. Nowhere does Lau show or suggest the use of anti-apoptotic proteins to enhance cytokine production.

C. Legal Standard of Obviousness

A modification which defeats the purpose of a primary reference, or renders it inoperative, cannot be considered obvious. *In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984), *In re Schulpen*, 157 USPQ 52 (CCPA 1968). Furthermore, in determining obviousness, "[I]t is not pertinent whether the prior art device possesses the functional characteristics of the claimed invention if the reference does not describe or suggest its structure." *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990).

Moreover, the Examiner is respectfully directed to *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 230 USPQ 416 (Fed. Cir. 1986) where the Federal Circuit held that a prior art reference should be considered as a whole, and portions arguing against or teaching away from the claimed invention must be considered. A reference teaches away if it leaves the impression that the product would not have the property sought by the applicant. *In re Caldwell*, 319 F.2d 254, 256, 138 USPQ 243, 245 (CCPA 1963).

As noted above, the specification of the Dixit. patent makes clear that maintaining *in vivo* cell viability is of paramount importance such that the cell may be used to inhibit infections, e.g. HIV. As taught throughout Dixit, cytokines such as TNF cause cell death, which is an undesirable event for maintaining *in vivo* viability. Dixit discloses that cells transfected with CrmA inhibit apoptosis, but nowhere does Dixit disclose that CrmA inhibits apoptosis such that more cytokine production would be desirable, or even acceptable, in any way. Furthermore, there is not teaching in Dixit of a way to increase cytokine production.

In contrast, the presently claimed invention is for the express purpose of increasing cytokine production, as described in the claims. Thus, the Dixit. reference teaches away because it does not dislose how one would increase cytokine production, and leaves the impression that increasing cytokine production would be undesirable. Furthermore, when the Dixit patent is considered as a whole, including the portion teaching away from the present invention, it is clear that the purpose of the Dixit. patent,

which is to maintain *in vivo* cell viability has been defeated in the present invention by increasing the production of cytokines.

Even assuming, arguendo, that the reference could have produced cytokines, it was at best, unappreciated. As such, it does not rise to the level of obviousness. It has long been established law that accidental, unintended and unappreciated production of a product does not constitute anticipation nor obviousness. In *Tilghman v. Proctor*, 102 U.S. 107 (1881), the Supreme Court upheld the validity of a patent even though small amounts of a product were produced by an earlier process. The Court of Customs and Patent Appeals has also held that a prior accidental or unwitting duplication of invention would not constitute a prior art reference for either §102 or §103. (citations omitted).

Furthermore, in *American Stainless Steel Company v. Rustless Iron Corp. of America*, 22 USPQ 114, 117-118 (4th Cir. 1934), the court stated, "The rule undoubtedly is that a prior use, in order to negative novelty in a patent, must be something more than an accidental or casual one. It need not have been persisted in and the thing produced need not have gone into commercial use; but at least the discovery must have gotten beyond the experimental stage and have become complete and the inventor must have understood and appreciated that it was capable of producing the results sought to be accomplished.

Here, there is no apparent recognition by Dixit nor Lau of the advantages of the present invention. Applicants submit that neither the Dixit reference, nor Lau, had any recognition that expressing an anti-apoptotic protein would be desirable for increased cytokine production From the Dixit reference's perspective, any such result would have been: (i) completely accidental; (ii) probably undesirable, because it certainly wouldn't lead to increased cell viability, and as discussed throughout the reference, would kill the cells; and, (iii) certainly unappreciated. Accordingly, under the standard articulated by the Supreme Court of the United States, the reference does not rise to the level of obviousness.

In conclusion, the Applicants submit that:

a) the modification proposed by Applicants defeats the purpose of the Dixit reference;

b) neither the Dixit, nor Lau *et al.* references show or suggest Applicants' cell line or composition;

c) taken as a whole, the Dixit reference teaches away from the claimed invention because it leaves the impression that the product sought by Applicants would not be desirable; and

d) even assuming the reference could be modified to enhance the production of cytokines as herein claimed, such a result would have been accidental, unintended, and unappreciated, and therefore cannot be considered obvious.

Thus, in the absence of any teaching of the problem, the desirability of a solution to the problem, or the nature of the solution as claimed herein, the claimed invention, as embodied in claims 1 or 3, cannot be considered obvious over the prior art.

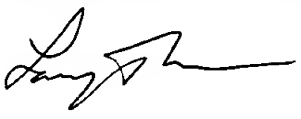
The remaining claims in the application patentably define over the prior art by their dependence on claims 1 and 3.

VII. Conclusion

In view of the above remarks, the applicants submit that the claims now pending are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4405.

Respectfully submitted,



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